

June 20, 1968

Dr. Bert M. Tolbert
Biophysicist, Biology Branch
Division of Biology and Medicine
U. S. Atomic Energy Commission
Washington, D. C. 20545

Dear Dr. Tolbert:

I note your letter of June 5 concerning the possible availability of C-13 with the deepest interest and enthusiasm.

I foresee a very large market for this isotope, probably exceeding that for deuterium, at least in its tracer uses. I do not know how to translate this into numerical terms on the scale of the world market. Nevertheless, the utility should be very large indeed. The area of most immediate interest to us in this department would be in density labeling of macromolecules for research on nucleic acids. I have no doubt at all, however, that this will come to have important diagnostic and pharmaceutical implications within the next ten years. Among the critical issues are, for example, the verification of vaccine viruses as chemically pure samples of the biological entity they are supposed to represent.

We are already deeply involved in the kind of instrumentation, especially mass spectrometry, which would be needed to exploit the availability of the C-13 isotope. I enclose a reprint that illustrates the use of a mass-label as a tracer for a specific functional group.

Access to quantitative analysis for C-13 may be the key to very large scale use of the isotope for tracer purposes in medicine. Your efforts towards the ready availability of the isotope should be accompanied by development work on methods of assay that would be accessible on a large scale. Very close attention should also be paid to the possibility that C-13 substitution may have unexpectedly large chemical effects on rigid or tightly caged cyclic molecules. This may also have its biological implications if the biological activity of steroids and similar hormones, exquisitely sensitive to the shape of the molecule, would be influenced by the substitution. Far from being a source of alarm about the utility of C-13, this may open the door to novel therapeutic adventures.

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To answer your specific questions, I would say that we might readily use as much as a kilogram of C-13, at the prices you mention, for current experimental work, and perhaps ten or a hundred times that amount over the decade.

Sincerely yours,

Joshua Lederberg
Professor of Genetics

P.S. I assume that you have made independent inquiry of Professor Kornberg here and Professor Meselson. I will transmit copies of your letter to some of my other colleagues for their independent comment.

copy of incoming letter to
Dr. Oseroff (with reply)
Dr. J. Rine
Dr. L. Styer
Dr. Dick Young (NASA)
Dr. Dorfman
Dr. Zaffaroni } *Syntex*